GLP-1 Receptor Agonists and Organ Outcomes in AL Amyloidosis

A Propensity Score-Matched Real-World Analysis of 1,122 Patients from the TriNetX Global Collaborative Network

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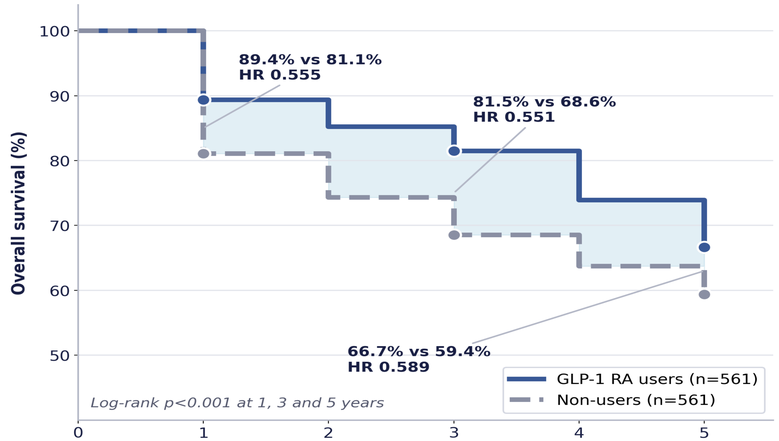
Background

- GLP-1 receptor agonists (GLP-1 RAs) reduce cardiovascular events in type 2 diabetes (LEADER, SUSTAIN-6) and in non-diabetic populations.
- Semaglutide reduced MACE by 20% in non-diabetic patients with established CVD and obesity (SELECT), and improved symptoms in non-diabetic HFpEF (STEP-HFpEF).
- These benefits are attributed to pleiotropic effects independent of glycaemic status.
- In AL amyloidosis, cardiac and renal injury arises from direct light chain fibril toxicity — not metabolic derangement.

Methods

- Design: Retrospective cohort, TriNetX Global Collaborative Network (173 healthcare organizations).
- Population: Adults (≥18 y) with AL amyloidosis (ICD-10 E85.81) diagnosed from January 2010; heredofamilial and wild-type ATTR excluded.
- Cohorts: GLP-1 RA users (n=561) vs non-users (n=561) after 1:1 propensity score matching on age, sex, comorbidities and concomitant medications.
- Primary endpoint: Overall survival. Secondary: cardiac, renal and haematological outcomes.
- Analysis: Kaplan-Meier with log-rank testing and Cox proportional hazards at 1-, 3- and 5-year horizons.

Survival

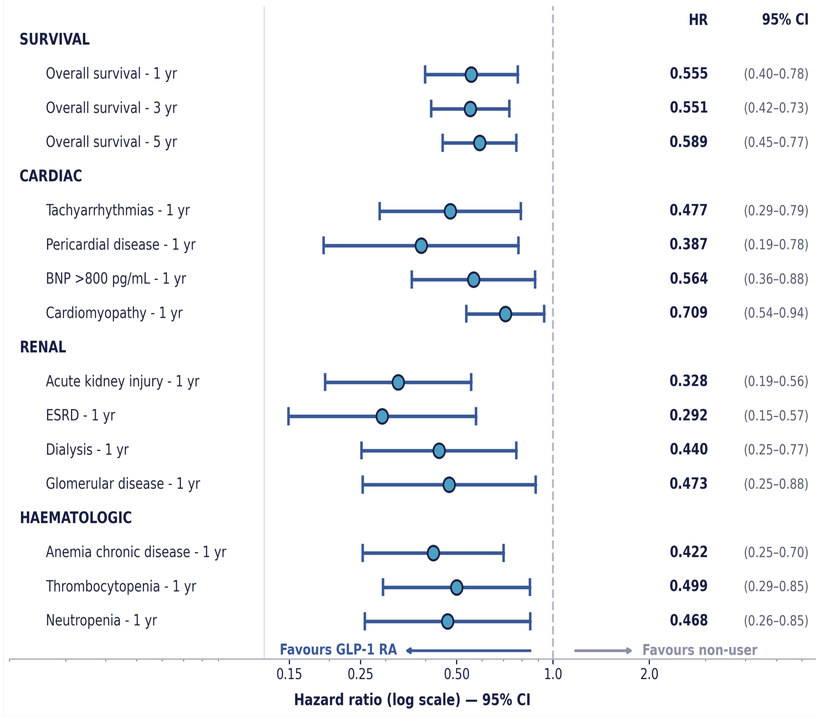


1 year	3 years	5 years
89.4%	**81.5%**	**66.7%**
vs 81.1%	vs 68.6%	vs 59.4%
HR 0.555 · p<0.001	HR 0.551 · p<0.001	HR 0.589 · p<0.001

Key results

- Survival: GLP-1 RA use was associated with superior overall survival at 1, 3 and 5 years (all p<0.001)
- Cardiac: Lower tachyarrhythmias (HR 0.477–0.621), pericardial disease (HR 0.387–0.465) and BNP >800 pg/mL (HR 0.525–0.564) at all timepoints; cardiomyopathy lower at 1 year (HR 0.709, p=0.015).
- Renal: AKI (HR 0.328–0.548), ESRD (HR 0.292–0.353), dialysis (HR 0.332–0.440) and glomerular disease (HR 0.473–0.547) lower at every timepoint (all p≤0.026).
- Haematological: Lower anemia of chronic disease, thrombocytopenia and neutropenia across all timepoints (all p≤0.015).
- No difference: Heart failure, heart block, ischemic heart disease and CKD did not differ significantly.

Outcomes by organ system



Conclusions

- In this propensity-matched real-world cohort, GLP-1 RA use in AL amyloidosis was associated with a sustained survival advantage across five years.
- Consistent reductions were observed in cardiorenal and haematological morbidity.
- These findings support prospective evaluation of GLP-1 RAs as adjunctive organ-protective therapy in AL amyloidosis.

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